

Predictive value of multiple imaging predictive models for spread through air spaces of lung adenocarcinoma: A systematic review and network meta-analysis

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 September 2023 and was last updated on 30 September 2023.

INTRODUCTION

Review question / Objective This study compared the predictive value of various imaging predictive models for STAS of LUAD through network meta-analysis.

Rationale Radiomics, the conversion of radiographic images into quantifiable information, holds the potential to enhance the accuracy of diagnosis, prognosis, and predictive models. Recent advancements in the predictive of STAS status in LUAD have demonstrated promising outcomes through the utilization of radiomics methods. However, in order to bridge the translational gap between radiomics as a scientific research tool and its clinical applicability, several challenges need to be addressed. These challenges encompass technical reproducibility, clinical validity, quantification, and cost-

effectiveness. Additionally, previous studies have exhibited heterogeneity in their approach, lacking a systematic investigation into the performance of radiomics in predicting STAS in LUAD. It is essential to identify the factors that influence the performance of radiomics in STAS predictive to enhance its clinical application further. Several radiomics models have been developed for the predictive of STAS using computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography/CT (PET/CT). These models have demonstrated varying performance, indicating heterogeneity. Consequently, our study aims to evaluate the risk of bias and methodological quality and conduct a network meta-analysis to assess the effectiveness of radiomics models in predicting preoperative STAS in LUAD. The findings from this study could provide valuable insights for clinicians, radiologists, and researchers involved in the

diagnosis and management of lung adenocarcinoma.

Condition being studied As a leading cause of cancer-related deaths worldwide, lung cancer, particularly lung adenocarcinoma (LUAD), might be linked to a distinctive invasion pattern. Beyond the infiltration of myofibroblast stroma and lymphovascular and pleural invasion, the spread through air spaces (STAS) is considered a novel invasion pattern in LUAD. STAS was initially identified as a potential form of lung tumor invasion by the Kadota study team. It was officially recognized as a novel manifestation of tumor spread in the 2015 classification by the World Health Organization. STAS is characterized by the presence of micropapillary clusters, solid nests, or individual cells extending beyond the tumor margin into the surrounding lung parenchyma air spaces. STAS, found in 14.8% to 56.4% of lung adenocarcinomas, has been associated with lower survival rates and a poorer prognosis when compared to STAS negative tumors. Furthermore, the presence of STAS holds potential in providing valuable clinical treatment information for patients diagnosed with lung adenocarcinoma. Multiple reports have highlighted a substantial risk of both local and distant recurrence in cases where sublobar resection was performed for tumors positive for STAS+. Conversely, patients who underwent lobectomy did not exhibit an increased risk of recurrence. Therefore, the early detection of STAS may hold notable clinical significance.

METHODS

Search strategy We conducted a comprehensive search using keywords such as "Risk factor," "Predictive," "spread through air spaces," "lung adenocarcinoma," "Computed Tomography," and "Nomograms" in databases including PubMed, Embase, and Web of Science to retrieve relevant literature. Additionally, we reviewed the references of the selected studies to ensure that no relevant publications were omitted.

Participant or population Inclusion criteria: ①Research subjects: LUAD patients diagnosed with STAS. ②Study constructs predictive model that can predict STAS in LUAD patients: It can reflect the accuracy, sensitivity (SEN) and specificity (SPE) of various predictive model for STAS in patients with LUAD.

Intervention The purpose of this study is to use network meta-analysis to compare the predictive performance of different imaging prediction models for STAS in early lung adenocarcinoma. And

diagnostic meta-analysis was used to evaluate the optimal prediction model.

Comparator The gold standard of STAS is pathological diagnosis, and this study uses its camera to evaluate the prediction performance of each prediction model.

Study designs to be included The extracted predictive models were categorized based on their distinct features, and a network meta-analysis (NMA) was conducted to evaluate their respective performance in predicting STAS. The aggregation and analysis of the NMA were performed using Stata software (Version-17.0) within a Bayesian framework, employing Markov Chain Monte Carlo Subset Simulation.

Eligibility criteria Exclusion criteria: ①Predictive models are not constructed based on radiological features; ②There were no clear inclusion and exclusion criteria in the study; ③Reviews and lecture-type literature. ④Literature for which the full text cannot be obtained. ⑤Literature for which data could not be extracted.

Information sources Databases including PubMed, Embase, and Web of Science to retrieve relevant literature. Additionally, we reviewed the references of the selected studies to ensure that no relevant publications were omitted.

Main outcome(s) The data extracted in this study primarily encompassed the following aspects: (1) Characteristics of the included literature, such as author information, publication time, country of origin, predictive models utilized, regression methods employed, and predictive factors investigated. (2) Characteristics of the study subjects, including sample size, gender distribution, and tumor stages. (3) Evaluation of effect indicators.

Quality assessment / Risk of bias analysis Regarding the included study, the research group followed the guidelines provided by the Cochrane Handbook and utilized the risk of bias assessment tool developed by the Cochrane Collaboration (RevMan v.5.3.5, Cochrane Collaboration, Oxford, UK). The methodological quality of the included studies was assessed from six different aspects, and judgments were made based on the categories of "yes" (indicating low bias), "no" (indicating high bias), or "unclear" (indicating a lack of relevant information or uncertainty regarding bias).

Strategy of data synthesis No data synthesis was required for this study.

Subgroup analysis Utilizing STATA, we performed subgroup diagnostic meta-analyses to evaluate the comparative predictive efficiency of various combined models. These models' efficacy was encapsulated by the area under the curve (AUC) of the summary receiver operating characteristics (sROC), providing an aggregated perspective of the results within each subgroup.

Sensitivity analysis The Relative Risk (RR) values and 95% confidence intervals (CI) of accuracy, SEN and SPE measured by different predictive models for STAS of LUAD were statistically analyzed, and the statistical differences were judged by calculation.

Language restriction None.

Country(ies) involved Xuzhou Cancer Hospital, China.

Keywords predictive models; lung adenocarcinoma; spread through air spaces; network meta-analysis.

Contributions of each author

Author 1 - Cong Liu performed the statistical analysis and wrote the manuscript.

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